

10/564,702

=> d his

(FILE 'HOME' ENTERED AT 13:53:23 ON 05 FEB 2009)

FILE 'REGISTRY' ENTERED AT 13:53:31 ON 05 FEB 2009

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 STRUCTURE UPLOADED

L4 0 S L3

L5 10 S L3 SSS FUL

L6 10 S L5 AND CAPLUS/LC

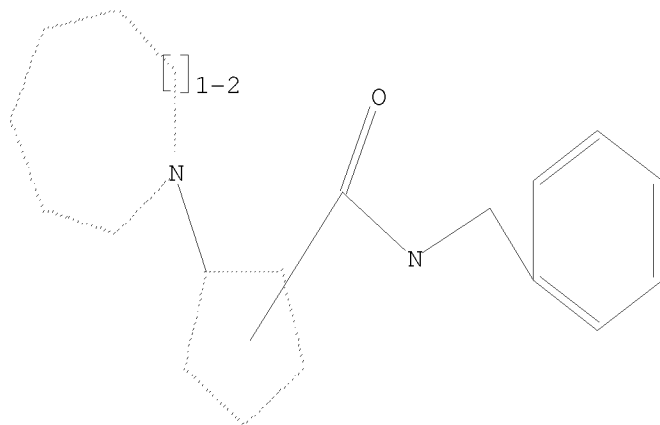
FILE 'CAPLUS' ENTERED AT 13:57:19 ON 05 FEB 2009

L7 2 S L6

=> d l3

L3 HAS NO ANSWERS

L3 STR



Structure attributes must be viewed using STN Express query preparation.

=> d ibib abs hitstr total

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:99600 CAPLUS

DOCUMENT NUMBER: 142:198060

TITLE: Preparation of 7 and 8 membered heterocyclic  
cyclopentyl benzylamide derivatives as modulators of  
chemokine receptor activityINVENTOR(S): Ge, Min; Goble, Stephen D.; Pasternak, Alexander;  
Yang, Lihu

PATENT ASSIGNEE(S): Merck &amp; Co., Inc., USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

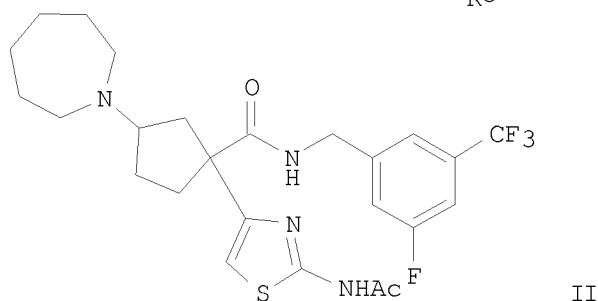
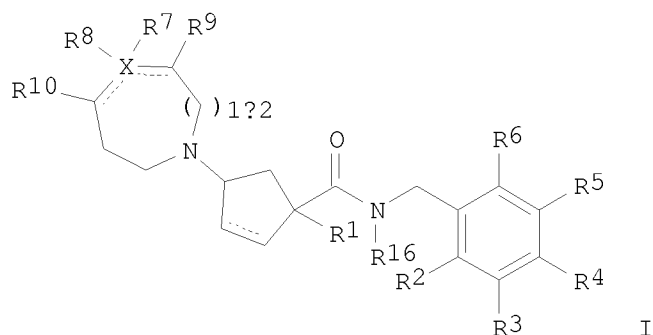
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO.  | DATE       |
|------------------------|--|----------|------------------|------------|
| WO 2005010154          | A2   | 20050203 | WO 2004-US21996  | 20040709   |
| WO 2005010154          | A3   | 20050825 |                  |            |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |          |                  |            |
| RW:                    | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                  |            |
| AU 2004259416          | A1   | 20050203 | AU 2004-259416   | 20040709   |
| CA 2532102             | A1   | 20050203 | CA 2004-2532102  | 20040709   |
| EP 1646392             | A2   | 20060419 | EP 2004-777832   | 20040709   |
| CN 1871012             | A  | 20061129 | CN 2004-80020467 | 20040709   |
| JP 2007523871          | T  | 20070823 | JP 2006-520232   | 20040709   |
| IN 2005DN06171         | A  | 20080509 | IN 2005-DN6171   | 20051230   |
| US 20060183731         | A1   | 20060817 | US 2006-564702   | 20060113   |
| PRIORITY APPLN. INFO.: |  |          | US 2003-487317P  | P 20030715 |
|                        |  |          | WO 2004-US21996  | W 20040709 |
| OTHER SOURCE(S):       | CASREACT 142:198060; MARPAT 142:198060   |          |                  |            |
| GI                     |  |          |                  |            |



AB N-benzylheterocyclylcyclopentanecarboxamide derivs. of the formula (I) and pharmaceutically acceptable salts thereof and individual diastereomers thereof [X = O, N, S, SO<sub>2</sub>, C; R<sub>1</sub> = H, C<sub>1</sub>-6 alkyl, -C<sub>0</sub>-6alkyl-O-C<sub>1</sub>-6alkyl, -C<sub>0</sub>-6 alkyl-S-C<sub>1</sub>-6-alkyl, - (C<sub>0</sub>-6-alkyl)(C<sub>3</sub>-7cycloalkyl)(C<sub>0</sub>-6alkyl), HO, heterocyclyl, cyano, etc.; R<sub>2</sub>, R<sub>4</sub>, R<sub>6</sub> = H, each (un)substituted C<sub>1</sub>-3 alkyl or -O-C<sub>1</sub>-3alkyl, HO, Cl, F, Br, Ph; R<sub>3</sub> = H, HO, halo, each (un)substituted C<sub>1</sub>-3 alkyl or NH<sub>2</sub>, etc.; R<sub>5</sub> = each (un)substituted C<sub>1</sub>-6 alkyl, -O-C<sub>1</sub>-6alkyl, -CO-C<sub>1</sub>-6alkyl, -S-C<sub>1</sub>-6alkyl, or 1-pyridyl, F, Cl, Br, (un)substituted -C<sub>4</sub>-6 cycloalkyl, etc.; R<sub>7</sub> = H, (C<sub>0</sub>-6-alkyl)phenyl, (C<sub>0</sub>-6alkyl)heterocycle, (C<sub>0</sub>-6-alkyl)-C<sub>3</sub>-7cycloalkyl, etc.; R<sub>8</sub> = H, nothing (when X is either O, S, SO<sub>2</sub>, or N or when a double bond joins the carbons to which R<sub>7</sub> and R<sub>10</sub> are attached), HO, C<sub>1</sub>-6 alkyl, C<sub>1</sub>-6-alkylhydroxy, -O-C<sub>1</sub>-3alkyl, (un)substituted CONH<sub>2</sub>, cyano; or where R<sub>7</sub> and R<sub>8</sub> may be joined together to form a ring such as 1H-indene, 2,3-dihydro-1H-indene, etc.; or R<sub>7</sub> and R<sub>9</sub> or R<sub>8</sub> and R<sub>10</sub> may be joined together to form an (un)substituted Ph or heterocycle ring; R<sub>9</sub>, R<sub>10</sub> = H, HO, hydroxy, C<sub>1</sub>-6 alkyl, C<sub>1</sub>-6 alkylhydroxy, -O-C<sub>1</sub>-3alkyl, oxo (when R<sub>9</sub> or R<sub>10</sub> is connected to the ring via a double bond), halo, etc.; R<sub>16</sub> = H, Ph, (un)substituted C<sub>1</sub>-6alkyl; the dashed line represents a single or a double bond] are prepared. These compds. are useful as modulators of chemokine receptor, in particular chemokine receptor CCR-2, for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease, in particular rheumatoid arthritis. Thus, reductive amination of 1-[2-[N-(tert-butoxycarbonyl)amino]thiazol-4-yl]-3-oxocyclopentane-1-carboxylic acid Et ester by hexamethyleneimine and NaBH(OAc)<sub>2</sub> in THF followed by alkali hydrolysis and acidification with AcOH gave 3-(Azepan-1-yl)-1-[2-[N-(tert-butoxycarbonyl)amino]thiazol-4-yl]cyclopentane-1-carboxylic acid which underwent amidation with 3-fluoro-5-(trifluoromethyl)benzylamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in the presence of 4-Dimethylaminopyridine and diisopropylethylamine in CH<sub>2</sub>Cl<sub>2</sub>,

followed by N-deprotection with CF<sub>3</sub>CO<sub>2</sub>H and N-acetylation with acetic anhydride to give N-[3-fluoro-5-(trifluoromethyl)benzyl]-3-(azepan-1-yl)-1-[2-(acetylamino)thiazol-4-yl]cyclopentane-1-carboxamide (II).

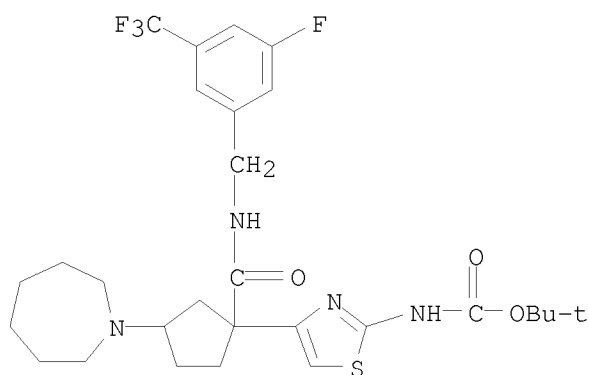
IT 835916-80-8P 835916-81-9P 835916-82-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of N-benzylheterocyclylcyclopentanecarboxamide derivs. as modulators of chemokine receptor for treating, ameliorating, controlling, or reducing risk of inflammatory and immunoregulatory disorder or disease)

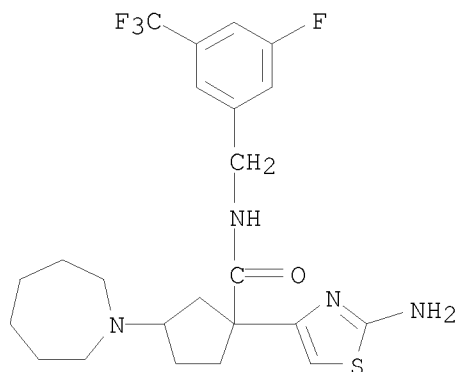
RN 835916-80-8 CAPLUS

CN Carbamic acid, [4-[1-[[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-3-(hexahydro-1H-azepin-1-yl)cyclopentyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 835916-81-9 CAPLUS

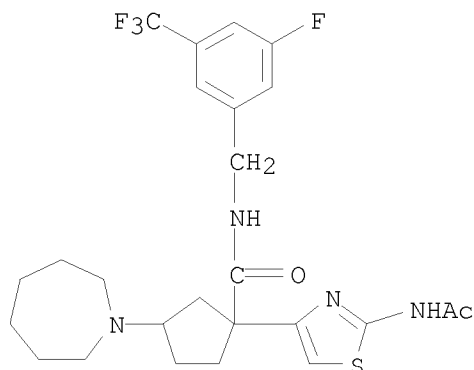
CN Cyclopentanecarboxamide, 1-(2-amino-4-thiazolyl)-N-[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1H-azepin-1-yl)- (CA INDEX NAME)



RN 835916-82-0 CAPLUS

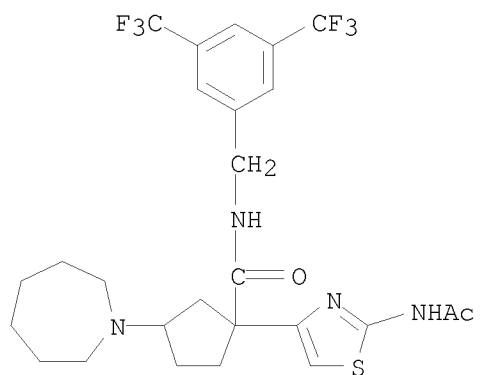
CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1H-azepin-1-yl)- (CA INDEX NAME)

NAME )



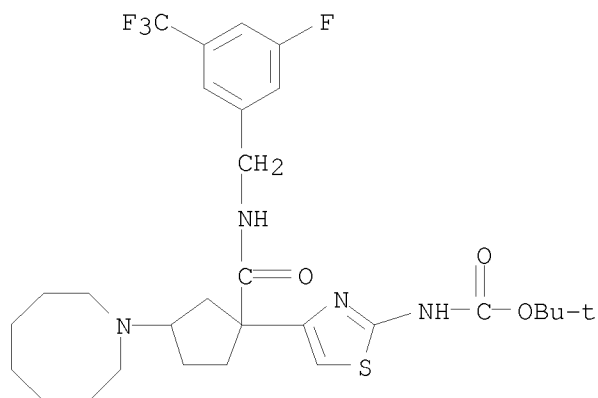
IT 690654-35-4P, N-[3,5-Bis(trifluoromethyl)benzyl]-3-(1-azepan-1-yl)-1-[2-(acetylamino)thiazol-4-yl]cyclopentane-1-carboxamide 835916-83-1P, N-[3-Fluoro-5-(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-[2-[(tert-butoxycarbonyl)amino]thiazol-4-yl]cyclopentane-1-carboxamide 835916-84-2P, N-[3-Fluoro-5-(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-(2-aminothiazol-4-yl)cyclopentane-1-carboxamide 835916-85-3P, N-[3,5-Bis(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-(2-aminothiazol-4-yl)cyclopentane-1-carboxamide 835916-86-4P, N-[3-Fluoro-5-(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-[2-(acetylamino)thiazol-4-yl]cyclopentane-1-carboxamide 835916-87-5P, N-[3,5-Bis(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-[2-(acetylamino)thiazol-4-yl]cyclopentane-1-carboxamide 835916-88-6P, N-[3,5-Bis(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-[2-(pivaloylamino)thiazol-4-yl]cyclopentane-1-carboxamide  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-benzylheterocyclylcyclopentanecarboxamide derivs. as modulators of chemokine receptor for treating, ameliorating, controlling, or reducing risk of inflammatory and immunoregulatory disorder or disease)

RN 690654-35-4 CAPLUS  
CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1H-azepin-1-yl)- (CA INDEX NAME)



RN 835916-83-1 CAPLUS

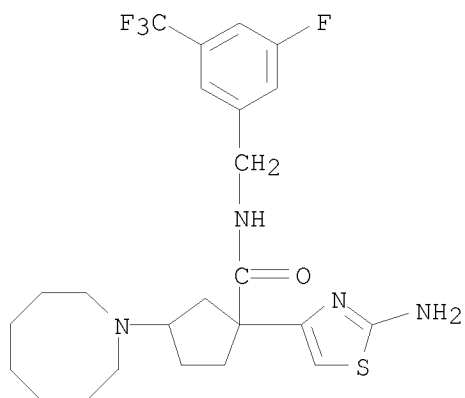
CN Carbamic acid, [4-[1-[[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-3-(hexahydro-1(2H)-azocinyl)cyclopentyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 835916-84-2 CAPLUS

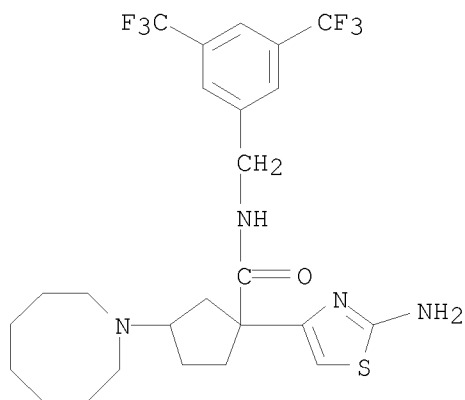
CN Cyclopentanecarboxamide, 1-(2-amino-4-thiazolyl)-N-[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)

10/564,702



RN 835916-85-3 CAPLUS

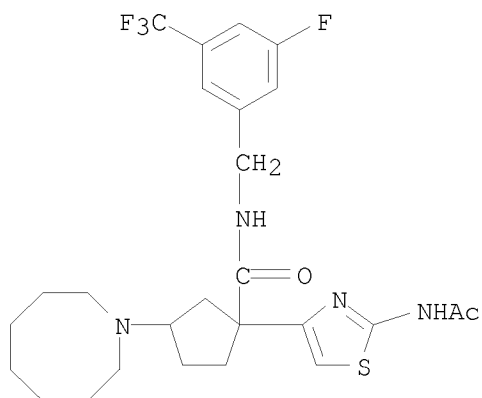
CN Cyclopentanecarboxamide, 1-(2-amino-4-thiazolyl)-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)



RN 835916-86-4 CAPLUS

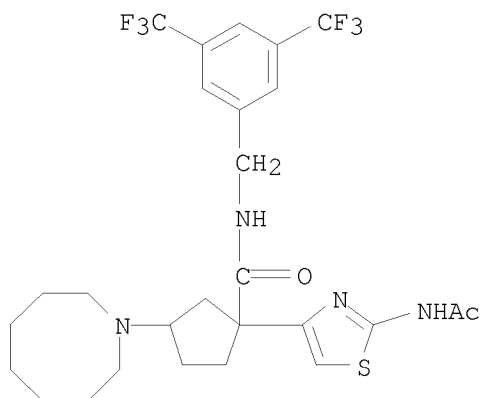
CN Cyclopentanecarboxamide, 1-[2-(acetamino)-4-thiazolyl]-N-[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)

10/564,702



RN 835916-87-5 CAPLUS

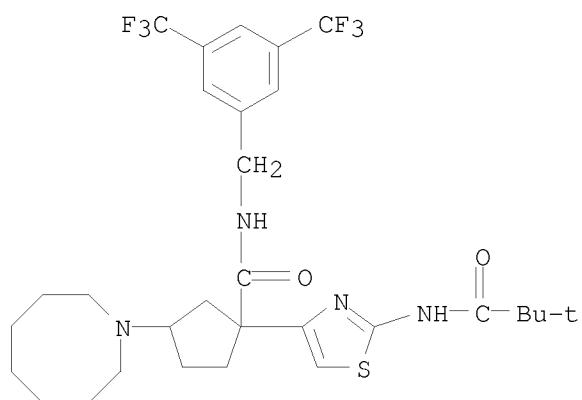
CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)



RN 835916-88-6 CAPLUS

CN Cyclopentanecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-1-[2-[(2,2-dimethyl-1-oxopropyl)amino]-4-thiazolyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)

10/564,702



REFERENCE COUNT:

1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:412749 CAPLUS

DOCUMENT NUMBER: 140:423705

TITLE: A preparation of piperidinylcyclopentyl amide derivatives, useful as modulators of chemokine receptor activity

INVENTOR(S): Zhou, Changyou; Pasternak, Alexander; Yang, Lihu

PATENT ASSIGNEE(S): Merck &amp; Co., Inc., USA

SOURCE: PCT Int. Appl., 100 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2004041163          | A2   | 20040521 | WO 2003-US34099 | 20031024   |
| WO 2004041163          | A3   | 20040715 |                 |            |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |            |
| CA 2503713             | A1   | 20040521 | CA 2003-2503713 | 20031024   |
| AU 2003284188          | A1   | 20040607 | AU 2003-284188  | 20031024   |
| EP 1558576             | A2   | 20050803 | EP 2003-776578  | 20031024   |
| R:                     | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK   |          |                 |            |
| JP 2006507301          | T  | 20060302 | JP 2004-550142  | 20031024   |
| US 20060173013         | A1   | 20060803 | US 2006-533337  | 20060330   |
| PRIORITY APPLN. INFO.: |  |          | US 2002-422381P | P 20021030 |
|                        |  |          | WO 2003-US34099 | W 20031024 |
| OTHER SOURCE(S):       | MARPAT 140:423705  |          |                 |            |
| GI                     |  |          |                 |            |

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to piperidinylcyclopentyl amide derivs. of formula I [wherein: X is -O-, -CH<sub>2</sub>O-, -CO<sub>2</sub>-, or -OC(O)-, etc.; W is (un)substituted Ph or heterocycle; Z is C, N, or O, wherein when Z is N, then R<sub>4</sub> is absent, and when W is O, then both R<sub>3</sub> and R<sub>4</sub> are absent; n = 0-4; R<sub>1</sub> is H, halo, trifluoromethyl, OH, alkyl, or CN, etc.; R<sub>2</sub> is (un)substituted C<sub>0</sub>-6alkyl-(phenyl/heterocycle); R<sub>3</sub> is (un)substituted C<sub>0</sub>-6alkyl-phenyl; R<sub>4</sub> is H, OH, CN, or alkyl, etc.; R<sub>5</sub> and R<sub>6</sub> are independently selected from H, OH, alkyl, alkoxy, or oxo, etc.; R<sub>3</sub> and R<sub>5</sub> or R<sub>4</sub> and R<sub>6</sub> may be joined together to form (un)substituted ring], useful as modulators of chemokine receptor activity. In particular, these compds. are useful as modulators of the chemokine receptor CCR-2. For instance, piperidinylcyclopentyl

amide derivative II (CCR-2 receptor binding  $IC_{50} < 1\mu M$ ) was prepared via amination of the obtained intermediate cyclopentanone derivative III by 4-(4-fluorophenyl)piperidine with a yield of 66% (example 1).

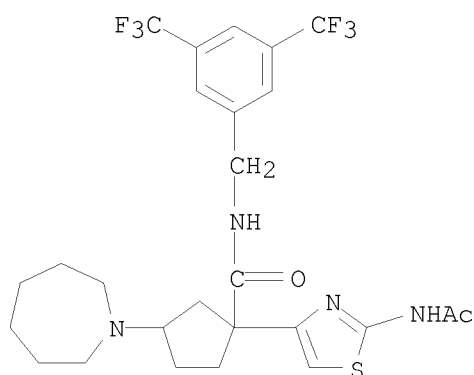
IT 690654-35-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidinylcyclopentyl amide derivs., useful as modulators of chemokine receptor activity)

RN 690654-35-4 CAPLUS

CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1H-azepin-1-yl)- (CA INDEX NAME)



REFERENCE COUNT:

1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT